Comparison of the Atkins, Zone, Ornish, and LEARN Diets for Change in Weight and Related Risk Factors Among Overweight Premenopausal Women

The A TO Z Weight Loss Study: A Randomized Trial

Christopher D. Gardner, PhD

Alexandre Kiazand, MD

Sofiya Alhassan, PhD

Soowon Kim, PhD

Randall S. Stafford, MD, PhD

Raymond R. Balise, PhD

Helena C. Kraemer, PhD

Abby C. King, PhD

THE ONGOING OBESITY EPI-demic,[1] along with its health costs and consequences[2] and the health benefits of weight loss,[3-6] have been well established. National dietary weight loss guidelines (ie, energy-restricted, low in fat, high in carbohydrate)[7] have been challenged, particularly by proponents of low-carbohydrate diets.[8,9] However, limited evidence has been available to effectively evaluate other diets.[10,11]

Several recent trials compared low-carbohydrate vs traditional low-fat, high-carbohydrate weight-loss diets.[12-16] A meta-analysis that pooled the results of these early trials concluded that low-carbohydrate, non–energy-restricted diets were at least as effective as low-fat, high-carbohydrate diets in inducing weight loss for up to 1 year.[17] However, most of these trials were limited by combinations of small sample sizes, high rates of attrition, short durations, or limited diet assessment.

For the A TO Z (Atkins, Traditional, Ornish, Zone) Weight Loss Study, we selected 4 diets—3 popular and substantially different diets and 1 diet based on national guidelines—representing a spectrum of carbohydrate intake: Atkins[8] (very low in carbohydrate), Zone[9]

Context Popular diets, particularly those low in carbohydrates, have challenged current recommendations advising a low-fat, high-carbohydrate diet for weight loss. Potential benefits and risks have not been tested adequately.

Objective To compare 4 weight-loss diets representing a spectrum of low to high carbohydrate intake for effects on weight loss and related metabolic variables.

Design, Setting, and Participants Twelve-month randomized trial conducted in the United States from February 2003 to October 2005 among 311 free-living, overweight/obese (body mass index, 27-40) nondiabetic, premenopausal women.

Intervention Participants were randomly assigned to follow the Atkins (n=77), Zone (n=79), LEARN (n=79), or Ornish (n=76) diets and received weekly instruction for 2 months, then an additional 10-month follow-up.

Main Outcome Measures Weight loss at 12 months was the primary outcome. Secondary outcomes included lipid profile (low-density lipoprotein, high-density lipoprotein, and non–high-density lipoprotein cholesterol, and triglyceride levels), percentage of body fat, waist-hip ratio, fasting insulin and glucose levels, and blood pressure. Outcomes were assessed at months 0, 2, 6, and 12. The Tukey studentized range test was used to adjust for multiple testing.

Results Weight loss was greater for women in the Atkins diet group compared with the other diet groups at 12 months, and mean 12-month weight loss was significantly different between the Atkins and Zone diets ($P<.05$). Mean 12-month weight loss was as follows: Atkins, –4.7 kg (95% confidence interval [CI], –6.3 to –3.1 kg), Zone, –1.6 kg (95% CI, –2.8 to –0.4 kg), LEARN, –2.6 kg (–3.8 to –1.3 kg), and Ornish, –2.2 kg (–3.6 to –0.8 kg). Weight loss was not statistically different among the Zone, LEARN, and Ornish groups. At 12 months, secondary outcomes for the Atkins group were comparable with or more favorable than the other diet groups.

Conclusions In this study, premenopausal overweight and obese women assigned to follow the Atkins diet, which had the lowest carbohydrate intake, lost more weight and experienced more favorable overall metabolic effects at 12 months than women assigned to follow the Zone, Ornish, or LEARN diets. While questions remain about long-term effects and mechanisms, a low-carbohydrate, high-protein, high-fat diet may be considered a feasible alternative recommendation for weight loss.

Trial Registration clinicaltrials.gov Identifier: NCT00079573

Author Affiliations: Stanford Prevention Research Center and the Department of Medicine, Stanford University Medical School, Stanford, Calif.
Corresponding Author: Christopher D. Gardner, PhD, Hoover Pavilion, N229, 211 Quarry Rd, Stanford, CA 94305-5705 (cgardner@stanford.edu).

(low in carbohydrate), LEARN[18] (Lifestyle, Exercise, Attitudes, Relationships, and Nutrition; low in fat, high in carbohydrate, based on national guidelines), and Ornish[19] (very high in carbohydrate). The primary study objective was to examine the effects of diets and gradations of carbohydrate intake on weight loss and related metabolic variables in overweight and obese premenopausal women.

METHODS

Participants

Participants were recruited from the local community, primarily through media advertisements. Premenopausal women aged 25 to 50 years were invited to enroll if their body mass index (calculated as weight in kilograms divided by height in meters squared) was 27 to 40, body weight was stable over the previous 2 months, and medications were stable for at least 3 months. Women were excluded if they self-reported hypertension (except for those whose blood pressure was stable using antihypertension medications); type 1 or 2 diabetes mellitus; heart, renal, or liver disease; cancer or active neoplasms; hyperthyroidism unless treated and under control; any medication use known to affect weight/energy expenditure; alcohol intake of at least 3 drinks/d; or pregnancy, lactation, no menstrual period in the previous 12 months, or plans to become pregnant within the next year. Race/ethnicity data were collected by self-report to be used for descriptive purposes and possible ancillary analyses of subgroups. All study participants provided written informed consent. The study was approved annually by the Stanford University Human Subjects Committee.

Intervention

Participants were enrolled in 4 cohorts, with the first cohort starting in February 2003 and the last cohort starting in September 2004. Randomization was conducted in blocks of 24 (6 per treatment group) and occurred by having a blinded research technician select folded pieces of paper with group assignments from an opaque enve-lope. Participants were assigned 1 of 4 diet books: *Dr Atkins' New Diet Revolution*,[8] *Enter the Zone*,[9] *The LEARN Manual for Weight Management*,[18] or *Eat More, Weigh Less* by Ornish.[19]

Each diet group attended 1-hour classes led by a registered dietitian once per week for 8 weeks and covered approximately one eighth of their respective books per class. The same dietitian taught all classes to all groups in all 4 cohorts and was rated by participants at the end of the 8-week sessions for enthusiasm and knowledge of the material (rating scale of 1-5, from "strongly disagree" to "strongly agree," respectively). The LEARN program is intended to be a 16-week program and, therefore, the 8 weeks of guidance through this book reflected an accelerated time frame, which was necessary to match the time frame given for the other 3 diet groups. Efforts to maximize retention in the study included e-mail and telephone reminders for appointments, e-mail or telephone contact from staff between the 2- and 6-month and between the 6- and 12-month data collection points, and incentive payments of $25, $50, and $75 for completing the 2-, 6-, and 12-month data collection, respectively.

Each group received specific target goals according to the emphasis of the assigned diet. The Atkins group aimed for 20 g/d or less of carbohydrate for "induction" (usually 2-3 months) and 50 g/d or less of carbohydrate for the subsequent "ongoing weight loss" phase. The Zone group's primary emphasis was a 40%-30%-30% distribution of carbohydrate, protein, and fat, respectively. The LEARN group was instructed to follow a prudent diet that included 55% to 60% energy from carbohydrate and less than 10% energy from saturated fat, caloric restriction, increased exercise, and behavior modification strategies. The primary emphasis for the Ornish group was no more than 10% of energy from fat. Additional recommendations given for physical activity, nutritional supplements, and behavioral strategies were consistent with those presented in each diet book.[8,9,18,19] The guidelines for the Zone and LEARN diets incorporated specific goals for energy restriction, while for the Atkins and Ornish diets, there were no specific energy restriction goals.

A range of behavior modification techniques were discussed during the 2-month classes. The Ornish and Zone books suggest some stimulus-control strategies but on the whole do not emphasize behavior modification, whereas both the Atkins and LEARN books suggest multiple strategies, such as relapse preparation and planning strategies and goal setting. Overall, the LEARN manual has the greatest emphasis on behavior modification strategies.

Process and Outcome Measures

All data were collected at baseline, 2, 6, and 12 months.

Diet and Physical Activity Data. Dietary intake data were collected by telephone-administered, 3-day, unannounced, 24-hour dietary recalls using Nutrition Data System for Research software, versions 4.05.33, 4.06.34, and 5.0.35 (Nutrition Coordinating Center, University of Minnesota, Minneapolis). Data collectors were trained and certified by the Nutrition Coordinating Center. The recalls occurred on 2 weekdays and 1 weekend day per time point, on nonconsecutive days whenever possible. Local foods not found in the comprehensive database were added to the database manually. A "food amounts booklet" was used to assist participants with portion size estimation. Energy expenditure was assessed using the well-established Stanford 7-day physical activity recall.[20]

Anthropometric Data. Height was measured to the nearest millimeter using a standard wall-mounted stadiometer. Body weight was measured to the nearest 0.1 kg on a calibrated clinical scale. Waist and hip circumference were measured to the nearest millimeter by standard procedures using a 150-cm anthropometric measuring tape.[21] Whole-body fat (percentage of body mass) was determined by dual-energy x-ray absorptiometry using pencil-beam mode on the Hologic QDR-2000 (first 3 cohorts) and, later, the

array mode on a Hologic QDR 4500 densitometer (last cohort) (Hologic Inc, Waltham, Mass).

Metabolic Measures. Blood samples were collected after a 10-hour or longer fast. Plasma total cholesterol and triglycerides (free glycerol blank subtracted) were measured enzymatically using Stanford Clinical Chemistry Laboratory–established methods.[22,23] High-density lipoprotein cholesterol (HDL-C) was measured by liquid selective detergent followed by enzymatic determination of cholesterol.[24] Low-density lipoprotein cholesterol (LDL-C) was calculated according to the methods described by Friedewald et al.[25] Lipid assays were monitored by the Lipid Standardization Program of the Centers for Disease Control and Prevention and were consistently within specified limits (monthly coefficients of variation were all ≤3.1%). The non–HDL-C measure was defined as total cholesterol value minus HDL-C value.[26] Total plasma insulin in serum was measured by radioimmunoassay.[27] Blood glucose was measured using a modification of the glucose oxidase/peroxidase method.[28,29]

Resting blood pressure was measured 3 times at 2-minute intervals as described elsewhere[30]; the initial reading was discarded and the last 2 readings were averaged. Clinic and laboratory staff members were blinded to treatment assignment.

Statistical Analyses

The primary objective was to test whether any of the 4 diets, representing a spectrum of carbohydrate intake, was more effective than any other in 12-month weight loss. The selected minimal clinically significant between-group difference in weight change was 2.7 kg (6 lb, approximately 3% for a 180-lb individual). Based on previous trials, we projected a 6.3-kg SD of weight change.[31,32] The primary analysis was conducted applying intention-to-treat methods with baseline values carried forward for missing values. Thus, with 4 treatment groups and a projected 75 participants per group, the study was designed to have 80% power

to detect a 2.7-kg difference for 12-month weight change between groups.

Dietary composition data (energy intake; percentage carbohydrate, fat, and protein; and grams of saturated fat and fiber) were analyzed using raw, unadjusted means (SDs) (ie, no imputation for missing data). Between-group differences in dietary intake at each time point were tested by analysis of variance (ANOVA). For weight and for all secondary outcome measures, analyses were conducted using all time points and all diets and were tested for diet group × time (log time +1) interactions in a mixed model using autoregressive covariance structure (SAS version 9.1.3 with Service Pack 3, SAS Institute Inc, Cary, NC). Triglyceride data were log-transformed to attain normal distributions for testing; for ease of interpretation, values presented in the text and figures are untransformed.

Differences among diets for 12-month changes from baseline were tested by ANOVA. For statistically significant ANOVAs, all pairwise comparisons among the 4 diets were tested using the Tukey studentized range adjustment. Statistical testing of changes from baseline to 2 months and to 6 months using pairwise comparisons are presented for descriptive purposes.

For exploratory purposes, ancillary analyses were conducted to determine the effect of diet group assignment on secondary outcomes at 12 months after adjusting for changes in weight loss using linear regression. Also for exploratory purposes, all analyses of weight and secondary outcome measures were tested using only available data, without using baseline values carried forward for missing data or other imputation methods. There were no substantive differences in any of these findings compared with the analyses with baseline values carried forward and, therefore, only the primary analyses are presented. Multiple regression was used to examine potential interactions between race/ethnicity and diet

Figure 1. Participant Flow Through the Trial
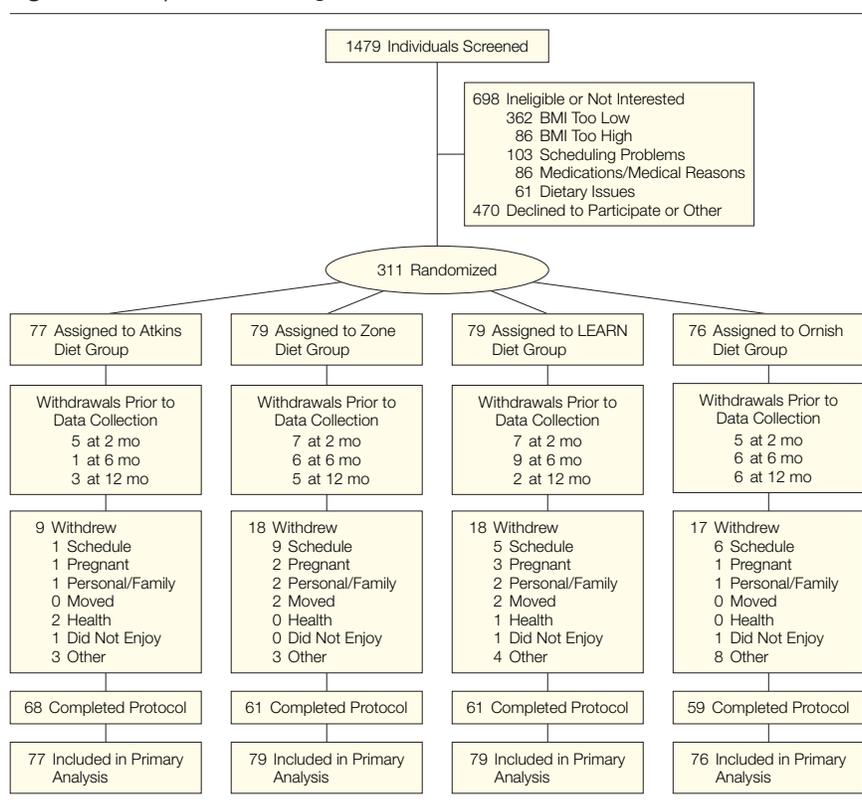
RESULTS

Participant enrollment began in February 2003, and the study ended in October 2005. **FIGURE 1** shows participant flow; **TABLE 1** shows baseline characteristics.

In all 4 diet groups, 85% to 89% of participants attended at least 75% of their assigned classes (≥6 of 8). Attendance was not different by diet group (*P* = .68). Retention at 12 months was 88%, 77%, 76%, and 78% for the Atkins, Zone, LEARN, and Ornish groups, respectively, and was not significantly different among groups (*P* = .30). Participant ratings for class instructor enthusiasm and knowledge of material were very high for both among all diet groups and were not significantly different among groups; average scores ranged from 4.4 to 4.7 on a scale of 1 to 5, with 5 as the highest rating.

Dietary Intake and Energy Expenditure

Total energy intake was not different among diet groups at baseline or any subsequent time point (*P* > .40 for all) (**TABLE 2**). However, relative to baseline, there was a significant mean decrease in reported energy intake at all postrandomization time points (*P* < .001): −497 (SD, 496), −387 (SD, 498), and −351 (SD, 576) kcal/d at 2, 6, and 12 months, respectively, for all groups combined.

There were no significant group differences at baseline in percentage of energy from carbohydrate, fat, or protein or in grams of saturated fat or fiber, except for a borderline significant difference in percentage of energy from fat between Atkins and LEARN (*P* = .05) (Table 2). At subsequent time points the diets were statistically different in carbohydrate content, progressing from low to high across the Atkins, Zone, LEARN, and Ornish groups. This same pattern was observed for fiber intake. The reverse pattern, higher to lower intakes, was statistically significant for protein, fat, and saturated fat at all time points. Between-group differences in patterns of nutrient intake were largest at 2 months. At 12 months, the patterns of nutrient differences between groups were still present, but the magnitude of differences was diminished.

Total energy expenditure was slightly higher for the Ornish group vs the other 3 groups at baseline but was not significantly different among groups at any subsequent time point (Table 1). Relative to baseline, there was a modest and significant mean increase (*P* < .05) in energy expenditure at all time points for all groups combined: +0.5 (SD, 2.8), +0.4 (SD, 2.7), and +1.0 (SD, 3.0) kcal/kg per day at 2, 6, and 12 months, respectively.

Weight and Anthropometric Outcomes

Mean 12-month weight change was −4.7 kg (95% confidence interval [CI], −6.3 to −3.1 kg) for Atkins, −1.6 kg (95% CI, −2.8 to −0.4 kg) for Zone, −2.2 kg (95% CI, −3.6 to −0.8 kg) for LEARN, and −2.6 kg (95% CI, −3.8 to −1.3 kg) for Ornish and was significantly different for Atkins vs Zone (**FIGURE 2**). At the 2- and 6-month intermediate time points, the weight change for the Atkins group was significantly greater than for all other groups (*P* < .05). Weight change among

Table 1. Baseline Participant Characteristics*

Characteristics	Atkins (n = 77)	Zone (n = 79)	LEARN (n = 79)	Ornish (n = 76)	All Diets (n = 311)
Demographics					
Age, y	42 (5)	40 (6)	40 (7)	42 (6)	41 (6)
Education, y	16 (2)	16 (2)	16 (2)	16 (2)	16 (2)
Race/ethnicity, No. (%)					
White	59 (76)	52 (66)	59 (75)	52 (69)	71
Black	2 (3)	7 (9)	6 (7)	4 (5)	6
Hispanic	7 (9)	8 (10)	7 (9)	11 (14)	11
Asian/Pacific Islander	7 (9)	9 (11)	6 (8)	8 (10)	10
Other	2 (3)	3 (4)	1 (1)	1 (1)	2
Smokers, No. (%)	2 (3)	4 (5)	4 (5)	3 (4)	4
Physical activity, kcal/kg per d	34 (6)	34 (6)	34 (5)	35 (7)	34 (6)
Anthropometrics					
Weight, kg	86 (13)	84 (12)	85 (14)	86 (10)	85 (12)
Body fat, %	41 (6)	40 (6)	38 (6)	40 (6)	40 (6)
Body mass index†	32 (4)	31 (3)	31 (4)	32 (3)	32 (4)
Waist-hip ratio	0.843 (0.067)	0.841 (0.068)	0.839 (0.066)	0.840 (0.060)	0.841 (0.065)
Cardiovascular disease risk factors					
LDL-C, mg/dL	109 (29)	114 (32)	104 (29)	111 (27)	110 (29)
HDL-C, mg/dL	53 (14)	52 (11)	51 (11)	50 (11)	52 (12)
Triglycerides, mg/dL	125 (78)	123 (98)	119 (73)	118 (62)	121 (78)
Non–HDL-C, mg/dL	134 (33)	139 (39)	127 (34)	135 (33)	134 (35)
Ratio of total cholesterol to HDL-C	3.7 (1.0)	3.8 (1.1)	3.6 (1.0)	3.8 (1.0)	3.7 (1.0)
Fasting insulin, μU/mL	10 (7)	10 (7)	10 (8)	10 (5)	10 (6)
Fasting glucose, mg/dL	92 (9)	94 (20)	96 (17)	93 (13)	94 (15)
Blood pressure, mm Hg					
Systolic	118 (11)	115 (13)	116 (12)	116 (10)	116 (11)
Diastolic	75 (8)	74 (9)	75 (9)	75 (8)	75 (8)
Metabolic syndrome, No. (%)‡	22 (29)	20 (25)	29 (37)	27 (36)	99 (32)

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
SI conversions: To convert LDL-C, HDL-C, and total cholesterol to mmol/L, multiply by 0.0259. To convert triglycerides to mmol/L, multiply by 0.0113. To convert glucose to mmol/L, multiply by 0.0555.
*Data are expressed as mean (SD) unless otherwise indicated.
†Calculated as weight in kilograms divided by height in meters squared.
‡Determined by criteria of ATP III.[33]

the Zone, LEARN, and Ornish groups did not differ significantly at any time point. The pattern of changes in body mass index, percentage of body fat, and waist-hip ratio among groups paralleled the changes in weight, although the between-group differences at 12 months did not achieve statistical significance for percentage of body fat (P = .07) or waist-hip ratio (P = .10) (TABLE 3).

Lipid Outcomes

Results generated by 84% of the study population (n = 262) with baseline blood samples (Atkins, n = 70; Zone, n = 65; LEARN, n = 63; and Ornish, n = 64) were available for testing. Four of the LDL-C values could not be calculated because of triglyceride concentrations greater than 400 mg/dL (4.52 mmol/L) and were treated as missing data. At all time points, the statistically significant findings for HDL-C and triglycerides concentrations favored the Atkins group (Table 3). Changes in LDL-C concentrations at 2 months favored the LEARN and Ornish diets over the Atkins diet; however, these differences diminished and were no longer significant at 6 and 12 months. Non-HDL-C differences among groups were not significant at any time point.

Insulin, Glucose, and Blood Pressure Outcomes

Insulin and glucose measurements were obtained from the same aforementioned 84% of the total sample for lipids. Neither the overall trajectory (ie, across all time points) nor the 12-month differences were significantly different among groups for either fasting insulin or fasting glucose concentrations (Table 3).

Parallel to the group changes in weight, the decrease in mean blood pressure levels was largest in the Atkins group at all time points. At 12 months, the decrease in systolic blood pressure was significantly greater for the Atkins group than for any other group. For diastolic pressure, the only significant pairwise difference at 12 months

favored the Atkins over the Ornish group.

Ancillary Analyses of Diet Group Effects Independent of Changes in Weight

For the 249 participants who completed the full 12-month protocol, we examined the independent effect of diet group on secondary outcomes after adjusting for 12-month changes in weight using linear regression. Each of the statistically significant 12-month differences between diet groups (ie, triglycerides, HDL-C, and systolic and diastolic blood pressure; Table 3) remained statistically significant after including weight loss in the model; however, the level of significance was diminished.

COMMENT

Compared with women who were assigned to follow diets having higher car-

Table 2. Mean Dietary Intake and Energy Expenditure by Diet Group and Time Point*

	Atkins	Zone	LEARN	Ornish	*P* Value†
Energy, kcal/d					
Baseline	1888 (512)	1975 (567)	1925 (553)	1850 (541)	.52
2 mo	1381 (345)	1455 (464)	1476 (448)	1408 (453)	.52
6 mo	1538 (401)	1503 (348)	1598 (418)	1553 (530)	.64
12 mo	1599 (494)	1594 (523)	1654 (492)	1505 (437)	.43
Carbohydrate (% energy)					
Baseline	45.6 (10.5)	47.1 (9.0)	48.3 (9.2)	47.9 (8.6)	.31
2 mo	17.7 (11.8)[a]	42.0 (8.5)[b]	49.3 (8.6)[c]	63.1 (11.0)[d]	<.001
6 mo	29.5 (14.5)[a]	43.7 (9.2)[b]	48.2 (8.6)[b,c]	53.4 (13.4)[c]	<.001
12 mo	34.5 (14.4)[a]	45.4 (11.1)[b]	47.2 (8.9)[b,c]	52.4 (12.3)[c]	<.001
Protein (% energy)					
Baseline	16.6 (4.1)	15.6 (3.3)	16.7 (3.9)	16.3 (3.1)	.21
2 mo	27.7 (5.5)[a]	23.7 (5.8)[b]	20.1 (4.8)[c]	16.9 (4.3)[d]	<.001
6 mo	22.4 (6.3)[a]	20.1 (5.2)[a,b]	18.4 (4.6)[b]	18.1 (4.8)[b]	<.001
12 mo	20.6 (5.3)[a]	20.0 (5.2)[a,b]	18.5 (4.6)[a,b]	18.3 (4.0)[b]	.02
Fat (% energy)					
Baseline	36.2 (7.8)[a]	35.6 (6.5)[a,b]	33.2 (7.2)[b]	35.1 (7.0)[a,b]	.05
2 mo	54.7 (9.0)[a]	34.8 (6.6)[b]	30.2 (7.3)[c]	21.1 (8.0)[d]	<.001
6 mo	47.0 (11.9)[a]	35.7 (7.3)[b]	31.3 (7.8)[c]	28.3 (10.7)[c]	<.001
12 mo	44.3 (12.5)[a]	34.5 (7.8)[b]	32.9 (7.1)[b]	29.8 (10.5)[b]	<.001
Saturated fat, g/d					
Baseline	26.5 (11.1)	27.0 (10.9)	24.3 (11.0)	24.8 (10.3)	.34
2 mo	30.7 (9.8)[a]	19.3 (10.3)[b]	16.8 (9.8)[b]	10.3 (7.8)[c]	<.001
6 mo	28.1 (11.1)[a]	20.5 (8.0)[b]	19.0 (8.9)[b,c]	16.2 (10.1)[c]	<.001
12 mo	27.2 (13.3)[a]	21.6 (11.2)[b]	20.1 (9.8)[b]	16.9 (11.4)[b]	<.001
Fiber, g/d					
Baseline	17.4 (6.6)	17.8 (8.7)	17.6 (7.5)	16.6 (6.6)	.79
2 mo	11.0 (6.3)[a]	16.9 (6.7)[b]	17.8 (7.1)[b]	22.1 (9.4)[c]	<.001
6 mo	14.0 (6.3)[a]	15.3 (7.6)[a,b]	16.7 (6.3)[a,b]	19.3 (11.1)[b]	.001
12 mo	15.2 (6.6)[a]	16.7 (9.4)[a,b]	18.3 (7.8)[a,b]	19.3 (9.4)[b]	.03
Energy expenditure, kcal/kg per d					
Baseline	33.7 (1.8)[a]	34.1 (2.6)[a]	33.9 (1.5)[a]	34.9 (3.2)[b]	.007
2 mo	34.6 (2.1)	34.5 (2.4)	34.8 (2.4)	34.7 (2.3)	.88
6 mo	34.3 (2.4)	34.4 (1.9)	34.8 (2.0)	34.6 (2.3)	.65
12 mo	34.8 (2.7)	35.4 (3.3)	35.6 (2.2)	35.8 (5.8)	.42

*Data presented are unadjusted raw data with no imputations for missing data. Standard deviations are presented in parentheses. Sample sizes for baseline and 2, 6, and 12 months, respectively, are: Atkins, n = 77, 73, 71, and 68; Zone, n = 79, 73, 67, and 57; LEARN, n = 79, 73, 66, and 60; and Ornish, n = 76, 72, 67, and 56.
†By analysis of variance.
[a,b,c,d] When the analysis of variance (last column) was statistically significant (P<.05), all pairwise comparisons among diet groups were tested for statistical significance using the Tukey studentized range test. Pairwise comparisons that were significantly different from one another are indicated by superscripts as follows: when the values for 2 diet groups within a row do not share a common superscript, they are significantly different, whereas if the values do share a common superscript, they are not significantly different.

Figure 2. Weight Change Relative to Baseline
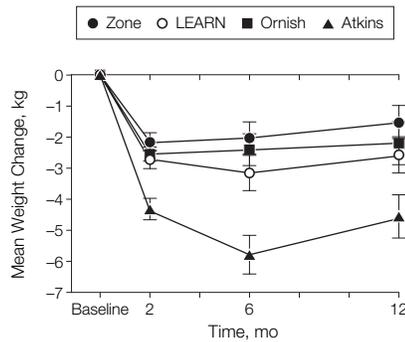
Baseline values were carried forward for any missing values. The overall diet group × time interaction was significant ($P<.001$). The analysis of variance test for differences among diet groups in weight change from baseline was significant at 2 and 6 months ($P<.001$), and at 12 months ($P=.01$). Analyses of all pairwise differences by the Tukey standardized range test ($<.05$) indicate that the Atkins diet group was significantly different than all other diet groups at 2 and 6 months and that the Atkins diet group was significantly different than the Zone diet group at 12 months. There were no significant differences among the Zone, LEARN, or Ornish diet groups at any time point. Error bars indicate standard error of the mean.

bohydrate content, women assigned to the diet with the lowest carbohydrate content had more weight loss and more favorable changes in related metabolic risk factors at 2 and 6 months. The finding of greater weight loss for the Atkins diet continued through 12 months, reaching statistical significance in comparison with the Zone diet. There were no significant differences in weight loss at any time point among the Zone, LEARN, and Ornish diets. Although the weight loss in the Atkins group was greater than that of other groups, the magnitude of weight loss was modest, with a mean 12-month weight loss of only 4.7 kg.

Many concerns have been expressed that low-carbohydrate weight-loss diets, high in total and saturated fat, will adversely affect blood lipid levels and cardiovascular risk.[34-36] These concerns have not been substantiated in recent weight-loss diet trials. The recent trials, like the current study, have consistently reported that triglycerides, HDL-C, blood pressure, and measures of insulin resistance either were not significantly different or were more favorable for the very-low-carbohydrate groups.[12-16]

The exception to this pattern has been LDL-C concentrations. Two of the most consistent findings in recent trials of low-carbohydrate vs low-fat diets have been higher LDL-C concentrations and lower triglyceride concentrations in the low-carbohydrate diets.[17] Although a higher LDL-C concentration would appear to be an adverse effect, this may not be the case under these study conditions. The triglyceride-lowering effect of a low-carbohydrate diet leads to an increase in LDL particle size, which is known to decrease LDL atherogenicity.[37-39] In the current study, at 2 months, mean LDL-C concentrations increased by 2% and mean triglyceride concentrations decreased by 30% in the Atkins group. These findings are consistent with a beneficial increase in LDL particle size, although LDL particle size was not assessed in our study. In addition, we examined non–HDL-C concentrations as an alternate indicator of atherogenic lipoproteins—a variable not substantially influenced by changes in triglyceride concentrations[26]—and observed no significant differences among groups at any time point.

Therefore, we interpret these findings to suggest that there were no adverse effects on the lipid variables for women following the Atkins diet compared with the other diets and, furthermore, no adverse effects were observed on any weight-related variable measured in this study at any time point for the Atkins group. Further examination of the dietary effects on lipid variables would benefit from analyses of lipoprotein particle subfractions and follow-up of longer than 12 months.

Our study and the study by Dansinger et al[16] were similar in several design features, including similar number and types of treatment groups and the same duration. Despite the similarities in design, several conclusions differed between the trials. Dansinger et al reported that weight loss at 12 months did not differ by diet group but only by level of adherence, regardless of diet type. In addition, Dansinger et al reported improvements within groups over 12 months for cardiac risk factors but did not report any significant differences between groups. In contrast, we observed statistically significant differences among diet groups for both weight loss and risk factors at 12 months.

These differences are likely attributable to at least 2 factors. One factor concerns the different study populations: our study was restricted to women aged 20 to 50 years who did not have diabetes and were not taking medications for cardiac risk factors, whereas the population in the study by Dansinger et al was much broader in its inclusion criteria. A second likely factor was differences in statistical power; in the study by Dansinger et al, 93 of 160 enrolled participants completed the trial (42% attrition at 12 months; ie, n=21-26 per treatment group); in the current study, 248 of 311 women completed the trial (20% attrition; ie, n=58-68 per treatment group).

The current study examined whether risk factor responses to diets were independent of weight loss. After statistically adjusting for weight loss differentials among groups, the secondary outcome differences among groups at 12 months that were significant in the unadjusted model remained significant in the adjusted model, although the level of significance was diminished. This supports a combined effect of benefit for the very-low-carbohydrate Atkins diet attributable to both increased weight loss and dietary composition. However, our study was not designed to specifically address this ancillary question. Krauss et al[38] recently addressed this issue directly in a study testing diets that ranged from low to high carbohydrate intake under conditions of weight stability followed by conditions of weight loss. Improvements in lipids and lipoproteins were greater for participants in the very-low-carbohydrate diet during the weight-stable phase but were greater for those in the high-carbohydrate diet

Table 3. Mean Changes in Secondary Outcomes Relative to Baseline, by Diet Group and Time*

	Atkins (n = 77)	Zone (n = 79)	LEARN (n = 79)	Ornish (n = 76)	P Value Overall Diet Group × Time†	12 Months‡
Body mass index§					<.001	
2 mo	−1.60 (0.98)	−0.76 (0.99)	−0.99 (1.00)	−0.95 (0.90)		
6 mo	−2.16 (2.14)	−0.73 (0.90)	−1.13 (1.91)	−0.85 (1.60)		
12 mo	−1.65 (2.54)[a]	−0.53 (2.00)[b]	−0.92 (2.00)[a,b]	−0.77 (2.14)[a,b]		.01
Body fat, %					.01	
2 mo	−2.1 (1.8)	−1.8 (2.0)	−1.5 (1.8)	−1.2 (1.5)		
6 mo	−3.6 (4.1)	−1.7 (3.1)	−2.0 (3.2)	−1.4 (2.7)		
12 mo	−2.9 (4.8)	−1.3 (3.4)	−1.0 (3.4)	−1.5 (4.0)		.07
Waist-hip ratio					.04	
2 mo	−0.019 (0.016)	−0.012 (0.019)	−0.012 (0.022)	−0.009 (0.019)		
6 mo	−0.021 (0.023)	−0.014 (0.023)	−0.010 (0.022)	−0.010 (0.023)		
12 mo	−0.019 (0.026)	−0.013 (0.023)	−0.009 (0.024)	−0.012 (0.024)		.10
LDL-C, mg/dL					.26	
2 mo	2.3 (23.5)	−5.3 (17.8)	−7.3 (20.8)	−10.1 (19.8)		
6 mo	1.7 (22.3)	0.5 (14.9)	−2.4 (19.4)	−3.2 (19.9)		
12 mo	0.8 (22.6)	0.0 (17.6)	0.6 (17.0)	−3.8 (19.0)		.49
HDL-C, mg/dL					.03	
2 mo	−0.4 (7.7)	−0.5 (5.4)	−3.8 (6.1)	−5.3 (9.0)		
6 mo	5.1 (9.6)	3.3 (6.9)	2.1 (6.7)	0.0 (9.2)		
12 mo	4.9 (9.1)[a]	2.2 (6.1)[a,b]	2.8 (7.7)[a,b]	0.0 (6.3)[b]		.002
Triglycerides, mg/dL					.003	
2 mo	−52.3 (66.8)	−24.8 (53.1)	−17.4 (48.9)	10.9 (55.0)		
6 mo	−35.6 (64.4)	−21.3 (58.9)	−16.1 (50.1)	−7.6 (54.4)		
12 mo	−29.3 (59.0)[a]	−4.2 (48.5)[b]	−14.6 (60.8)[a,b]	−14.9 (46.2)[a,b]		.01
Non–HDL-C, mg/dL					.92	
2 mo	−8.0 (26.3)	−10.2 (21.7)	−10.7 (19.0)	−7.8 (17.8)		
6 mo	−4.7 (23.1)	−3.7 (18.8)	−5.6 (18.6)	−4.7 (22.1)		
12 mo	−5.1 (22.5)	−0.5 (20.0)	−4.0 (19.7)	−6.8 (20.3)		0.36
Insulin, µU/mL					.23	
2 mo	−3.0 (3.9)	1.0 (6.0)	−1.9 (4.7)	−1.1 (3.3)		
6 mo	−2.8 (4.1)	0.1 (8.9)	−2.1 (5.4)	−0.1 (3.6)		
12 mo	−1.8 (4.8)	−1.5 (4.9)	−1.8 (5.1)	−0.2 (3.8)		.17
Glucose, mg/dL					.77	
2 mo	−0.4 (6.8)	−1.6 (10.6)	−0.8 (8.3)	−1.4 (6.9)		
6 mo	0.2 (7.6)	−1.7 (9.6)	−0.9 (9.9)	−0.6 (7.3)		
12 mo	−1.8 (13.4)	−1.6 (6.5)	0.5 (9.2)	−0.8 (7.9)		.54
Systolic blood pressure, mm Hg					.001	
2 mo	−6.8 (8.0)	−3.2 (8.2)	−3.6 (6.9)	−1.6 (6.3)		
6 mo	−6.4 (9.5)	−3.6 (8.0)	−4.3 (7.6)	−1.7 (7.0)		
12 mo	−7.6 (11.0)[a]	−3.3 (8.1)[b]	−3.1 (9.3)[b]	−1.9 (7.7)[b]		<.001
Diastolic blood pressure, mm Hg					.03	
2 mo	−2.9 (6.2)	−2.1 (5.6)	−1.4 (4.4)	−0.4 (5.5)		
6 mo	−3.3 (6.9)	−1.8 (5.6)	−2.5 (5.8)	−1.0 (5.6)		
12 mo	−4.4 (8.4)[a]	−2.1 (5.8)[a,b]	−2.2 (6.7)[a,b]	−0.7 (6.0)[b]		.009

SI conversions: To convert LDL-C, HDL-C, and total cholesterol to mmol/L, multiply by 0.0259. To convert triglycerides to mmol/L, multiply by 0.0113. To convert glucose to mmol/L, multiply by 0.0555.

*Intention-to-treat analysis, with baseline data carried forward for missing values. Standard deviations are presented in parentheses. For LDL-C, HDL-C, triglyceride, non–HDL-C, insulin, and glucose data, results are presented for those with available blood sample data (84% of full sample): Atkins, n = 70; Zone, n = 65; LEARN, n = 63; and Ornish, n = 64.

†P value for diet group × time interaction, determined using mixed-model and autoregressive covariance structure.

‡P values for 12-month change from baseline results, determined by analysis of variance.

§Calculated as weight in kilograms divided by height in meters squared.

[a,b]For a given outcome measure at the 12-month time point, when the analysis of variance (last column) was statistically significant (P<.05), all pairwise comparisons among diet groups were tested for statistical significance using the Tukey studentized range test. Pairwise comparisons that were significantly different from one another are indicated by superscripts as follows: when the values for 2 diet groups within a row do not share a common superscript, they are significantly different, whereas if the values do share a common superscript, they are not significantly different.

after weight loss and restabilization; overall the low-carbohydrate and weight-loss effects were reported to be equivalent but not additive under the tightly controlled conditions of this study.

The 4 study diets used in our study differed significantly in composition beyond carbohydrate content. Protein, fat, and saturated fat followed a continuum across diets, inverse to carbohydrate content. In a series of recent weight-loss trials that substituted either protein for fat while holding carbohydrate constant[40,41] or protein for carbohydrate while holding fat constant,[38,42,43] the higher-protein diets led to improvements in weight loss, triglycerides, and HDL-C and increased satiety. In the OmniHeart study, under weight-stable conditions, blood pressure–lowering benefits were observed for a high-protein relative to a high-carbohydrate diet.[44] Therefore, the reported effects of the current study should be interpreted as resulting from the combination of macronutrient changes that occur when following low- vs high-carbohydrate diets, not just changes in carbohydrates alone. For example, greater satiety from the higher protein content of the Atkins diet may have contributed to the benefits observed for that group, although satiety was not assessed.

The amount of weight loss at 12 months relative to baseline among all groups was modest at 2% to 5%. However, even modest reductions in excess weight have clinically significant effects on risk factors such as triglycerides and blood pressure and, therefore, can have an important public health impact at the population level.[4-6,45,46] Greater success with long-term weight loss is likely dependent on a number of factors beyond macronutrient composition, including improved behavioral strategies, longer-term structured guidance, greater emphasis on increasing energy expenditure (ie, regular physical activity), and addressing societal and environmental factors, such as portion sizes of restaurant meals.[45,47-49]

Strengths of the current study relative to previous trials include a larger sample size, a 12-month duration, lower attrition rates, the contrast of 4 rather than 2 diets differing in carbohydrate content, and the significant differences in macronutrient intake achieved by the diet groups. Although adherence to the 4 sets of dietary guidelines varied within each treatment group and waned over time, especially for the Atkins and Ornish diets, we believe that the adherence levels obtained are a fair representation of studying the diets and variations in macronutrient intake under realistic conditions and, therefore, increase the external validity of the findings. Other strengths include the extensive dietary assessment and the comprehensive health and risk factor data collected. The restriction of our study to premenopausal women allowed us to avoid possible interactions of effects with sex and menopausal status, but because of our focus on this population, generalizations of findings to other populations should be made with caution.

This study also has several limitations. Menstrual cycle timing was not taken into consideration for blood sampling for lipid analyses, which likely increased within-person variability and diminished the ability to detect between-group differences. Moreover, weight-loss trajectories for each group had not stabilized at 12 months; the trajectories of weight change between 6 and 12 months suggest that longer follow-up would likely have resulted in progressively diminished group differences. Other limitations included the lack of a valid and comparable assessment of individual adherence to the 4 different diets, the lack of data on whether participants had familiarity using any of the specific study diets prior to enrolling in the trial, and the lack of assessment of satiety.

CONCLUSIONS

In this study of overweight and obese premenopausal women, those assigned to follow the Atkins diet had more weight loss and more favorable outcomes for metabolic effects at 1 year than women assigned to the Zone, Ornish, or LEARN diets. Concerns about adverse metabolic effects of the Atkins diet were not substantiated within the 12-month study period. It could not be determined whether the benefits were attributable specifically to the low carbohydrate intake vs other aspects of the diet (eg, high protein intake).

While questions remain about long-term effects and mechanisms, these findings have important implications for clinical practice and health care policy. Physicians whose patients initiate a low-carbohydrate diet can be reassured that weight loss is likely to be at least as large as for any other dietary pattern and that the lipid effects are unlikely to be of immediate concern. As with any diet, physicians should caution patients that long-term success requires permanent alterations in energy intake and energy expenditure, regardless of macronutrient content.

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Table 4, the Reynolds Risk Score correctly results in an absolute increase in the number who would be recommended for treatment when thresholds are set at either 20% 10-year risk or at 10% 10-year risk, thus achieving a net clinical benefit. As with any risk classification system, perfect prediction will not be achieved, but an overall improvement in the targeting of prescription drugs to those women with the most appropriate levels of risk should help maximize benefits while minimizing cost and toxicity. Wang et al are also concerned about the use of self-reported blood pressure, weight, diabetes, and smoking. However, these variables show a similar magnitude of prediction in our data as in other major studies.

With regard to comments from Dr Stevens and Ms Coleman, while Table 5 compares fit using the model most often used in clinical practice, Table 4 shows superiority of the new models built using the same population and outcome definition. We acknowledge that external validation, using different cohorts, would be a useful next step. It is true that the Hosmer-Lemeshow statistic can be considered a general measure of goodness of fit.[1] However, since it directly compares observed with expected events, it is more sensitive to recalibration than most other measures, particularly the c-statistic, and is often treated as a measure of calibration.[2]

We do not concur with Dr Daniels and colleagues that epidemiologic data on natriuretic peptides support the use of this biomarker in healthy populations. Of the articles cited, most included prevalent myocardial infarction at baseline or evaluated elderly cohorts without adequate exclusion of prior cardiovascular events. More recent data suggest that B-type natriuretic peptide does not predict cardiovascular events among those free of disease at baseline.[3]

Paul M Ridker, MD
pridker@partners.org
Nancy R. Cook, ScD
Brigham and Women's Hospital
Boston, Massachusetts

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CORRECTIONS

Incorrect Wording and Data Error: In the Original Contribution entitled "Comparison of the Atkins, Zone, Ornish, and LEARN Diets for Change in Weight and Related Risk Factors Among Overweight Premenopausal Women: The A TO Z Weight Loss Study: A Randomized Trial" published in the March 7, 2007, issue of *JAMA* (2007;297(9):969-977), a sentence was incorrectly worded in the abstract, and data were reported incorrectly in the text. On page 969, in the "Conclusions" section of the abstract, the first sentence should have read "In this study, premenopausal overweight and obese women assigned to follow the Atkins diet, which had the lowest carbohydrate intake, had lost more weight at 12 months than those assigned to the Zone diet, and had experienced comparable or more favorable metabolic effects than those assigned to follow the Zone, Ornish, or LEARN diets." On page 972, in the last paragraph, the mean 12-month weight changes for the LEARN and Ornish diets were reversed: for LEARN it should have been −2.6 kg (95% CI, −3.8 to −1.3 kg) and for Ornish it should have been −2.2 kg (95% CI, −3.6 to −0.8 kg).

Incorrect Prevalence: In the Editorial entitled "Mandatory HPV Vaccination: Public Health vs Private Wealth" published in the May 2, 2007, issue of *JAMA* (2007; 297(17):1921-1923), 2 sentences regarding HPV prevalence were inaccurate. On page 1921, in the second paragraph, the second to last sentence should read: "Although infection with high-risk HPV types . . . high-risk types 16 and 18 have a relatively low prevalence (2.3% among screened females),[4] and not all women. . . . " Also on page 1921, second column, the last paragraph on the page should read: "Given that the overall prevalence of HPV vaccine types associated with cervical cancer is relatively low (2.3%). . . . "